Declaration pursuant to 37 C.F.R. § 1.132 ("Rule 132 Declaration") executed by Qing Qi, an inventor of the present invention, evidencing the factual statements set forth below.

The Examiner stated that Shinpo discloses, in part, the steps of: (1) hot water extraction of Spirulina; (2) centrifuging the hot water extract and obtaining the supernatant; (3) filtering the filtrate through a semi-permeable membrane; (4) DEAE-cellulose chromatography; and (5) obtaining a glycoprotein containing a single component.

The present invention discloses and claims, in part, the steps of: (a) dissolving a dry powdered Spirulina in 5-20 times water by weight and breaking the Spirulina cell walls; (b) heating a solution obtained from step (a) at 60°-100°C, and cooling the heated solution to separate a liquid phase from the solution; (c) adjusting pH of said liquid phase to 3.8-4.2, and filtering said liquid phase to obtain a filtrate; and (d) adjusting the filtrate to pH 7, and concentrating the filtrate.

As noted by the Examiner, the claims of the present invention differ from Shinpo in that Shinpo does not disclose the step of selective precipitation at pH 3.8-4.2 to remove specific impurities. However, the Examiner considered the presently claimed invention an obvious optimization of Shinpo's process stating that "the artisan of ordinary skill clearly would have recognized that performing pH values would affect the properties of the resulting product." The Examiner further invited

the Applicant to submit evidence of "unexpected results coming from the claimed extraction pH" to overcome this rejection.

With respect to the claimed extraction pH, the inventors of the presently claimed invention have found that selective precipitation of Spirulina at different pH levels results in the recovery of different proteoglcyan extracts having different biochemical characteristics. Rule 132 Declaration at ¶ 6. As shown in experiment 1.1 of Exhibit A to the attached Rule 132 Declaration, Spirulina precipitated at three different pH levels (*i.e.* pH 4, pH 5-6, and pH 8-9) produced main peaks and retention times for the resulting proteoglycan extracts which varied greatly using High Performance Liquid Chromatography (HPLC) analysis. Rule 132 Declaration at ¶ 7. In addition, as shown in experiment 1.2 of Exhibit A to the attached Rule 132 Declaration, Spirulina precipitated at three different pH levels produced different results in therapeutic efficacy of the resulting proteoglycan extracts using a pharmacodynamic assay. Furthermore, some of the therapeutic effects decreased significantly, and even disappeared in direct correlation to the pH level at which the proteoglycan extracts were precipitated. Rule 132 Declaration at ¶ 8.

Accordingly, the selective precipitation of Spirulina at the claimed pH produces unexpected results that would not have been obvious from Shinpo.

The claims of the present invention are also distinguishable from Shinpo because, as noted by the Examiner, "Shinpo does not explicitly disclose a cell wall breaking step." Rather, Shinpo discloses hot water treatment which the Examiner

claims "would have been expected to have broken at least a few cell walls." The Examiner invited the Applicants to submit evidence that the claimed cellular wall breaking step results in a different product than that suggested by Shinpo.

As shown in Exhibit "B" to the attached Rule 132 Declaration, the inventors of the presently claimed invention performed experiments to compare the extracted components from Spirulina cells using hot water treatment and ultrasonic treatment. In each of the examples using ultrasonic treatment, the concentration of proteoglycan in the extracted product was significantly greater than that of saccharide and protein. Whereas, in each of the examples using hot water treatment in accordance with the cited prior art, the concentration of proteoglycan in the extracted product was less than the amount of saccharide and significantly less than the amount of protein extracted. Rule 132 Declaration at ¶ 11. In addition, it was found that the 50% inhibition concentration (IC_{50}) for proteoglycan extracts resulting from ultrasonic treatment is significantly lower than that of proteoglycan extracts using hot water treatment. Rule 132 Declaration at ¶ 12.

Based on the foregoing, breaking the cellular walls of Spirulina using a cellular wall breaking method according to the present invention, such as by ultrasonic treatment, rapid stirring, osmotic pressure changing lysis, or enzymolysis, permits the removal of a product from Spirulina cells having greater quantities of proteoglycan as opposed to hot water treatment. Rule 132 Declaration

at ¶ 13. Accordingly, the cellular wall breaking step of the present invention produces unexpected results that would not have been obvious from Shinpo.

For the above reasons provided above, it is respectfully submitted that pending claims 1, 3-6, 8, 10-13, 15, 17-20, 22, 24-27, 29, 31-34, 36, 38-41, 43, 45-48, 50, 52-55, 57-61, and 63-71 are patentable over the cited prior art and are in condition for allowance. Accordingly, reconsideration and allowance of the pending claims is respectfully requested.

If the Examiner does not believe that the claims are in condition for allowance, the Examiner is respectfully requested to contact the undersigned at 215-568-6400.

Respectfully submitted,

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Enclosure